## REPLY: Neglecting Enterococci May Lead to a Misinterpretation of the Consequences of Last Changes in Endocarditis Prophylaxis American Heart Association Guidelines

We would like to thank Dr. Pericas and colleagues for their interest in our paper (1). We agree that enterococcus as an etiology of infective endocarditis (IE) is important due to increasing prevalence of IE (2) and evolving resistance to antibiotics. Hence, we do appreciate the suggestion to look at enterococcus as a specific subgroup and will include it in a future analysis. Monitoring the trend in enterococcal endocarditis will provide better insights into IE epidemiology and may have important implications in the prevention of IE.

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## Vasa Vasorum

### Still an Invisible Factor?

We read with great interest the paper by Taruya et al. (1) in a previous issue of the *Journal*. The authors should be congratulated for their detailed work. Utilizing as an imaging modality the light-based optical coherence tomography (OCT), they have shown that vasa vasorum (VV) and intraplaque neovascularization structure volumes differ between various plaque characteristics. In particular, the VV volume is positively correlated with fibrous plaque volume, whereas specific 3-dimensional structures of intraplaque neovessels are associated with plaque vulnerability.

Although we think that this work represents a significant contribution to the field of VV, we have some comments regarding the findings and their interpretation.

On the basis of our findings, we believe that images of VV and intraplaque neovessels obtained during the short time interval of 2 to 3 s (pull back imaging with OCT) represent only a part of the total VV and intraplaque neovessel existing network (external and internal) that nourishes the atherosclerotic plaque (2). Indeed, we have shown in an almost operator-independent quantitative analysis of contrast-enhanced intravascular ultrasound that maximal perfusion of the coronary atherosclerotic plaque through the existing VV network occurs at 20 s post-intracoronary contrast injection (2). Therefore, the obtained images and calculated volumes of VV and intraplaque neovessels may not reflect the total volume that perfuses the plaque, and as a result, correlations between study volumes of VV and atherosclerotic plaques may not be ideal. Furthermore, apart from the increased intracoronary pressure produced by continuous contrast infusion during OCT imaging on neovessel volume, rheological intraluminal conditions can be instantly altered by hemodynamics and heart movement, leading to constant fluctuation of volume. Additionally, the flashed x-ray contrast may influence the image that is received and analyzed further off-line, by interacting within the studied microvessels, as the analyzed frame is captured simultaneously with flashing.

The findings of Taruya et al. (1) add significant information to previously published data indicating the key role of neovascularization within the atherosclerotic plaque (3). Doubtless, VV neovascularization imaging and assessment, either with OCT or contrast-enhanced intravascular ultrasound, can be established as a valuable tool for vulnerable plaque detection and its therapeutic regression.

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## REPLY: Vasa Vasorum

### Still an Invisible Factor?

We deeply thank Drs. Vavuranakis, Kalogeras, and Tousoulis for their interest in our recent paper (1). Any current intravessel optical coherence tomography (OCT) systems require injection of flushing medium, resulting in high pressure in the arterial lumen and consequently within the arterial wall. As we mentioned in the limitations section of our paper, intramural pressure gradient can result in compression of some of the vasa vasorum (VV) and intraplaque neovessels (2). Therefore, the images obtained of VV and intraplaque neovessels may not precisely reflect the same pressure condition. However, the high pull back speed (20 cm/s) of frequency-domain OCT brought about the short time period for maximal pressure flushing. Keeping in mind the variable volume of the VV and intraplaque neovessels, we analyzed all images for region of interest. It may not be necessary to determine ideal perfusion pressure because the correlations would likely be similar under the same conditions.

Contrast-enhanced ultrasound (CEUS) is also available for analyses of neovessels. Previously published data indicate that CEUS provides a significant increase in the signal-to-noise ratio and might permit enhanced identification of the vasculature within the vessel walls and within the plaque (3). However, for coronary arteries, the spatial resolution of CEUS seems to be enough for adventitial VV but unsatisfactory to depict intraplaque neovessels.

We agree that future studies are needed in the same segment and lesion to assess the serial role of the VV and neovessels. We think that the 3-dimensional structure transition of VV and intraplaque neovessels might have a clinical application to determine the progression of atherosclerotic plaque, whether using frequency-domain OCT or CEUS.

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